

In the Claims

1 (currently amended). A pharmaceutical co-crystal composition, comprising: an API and a co-crystal former, wherein:

- a) the API is a liquid or a solid at room temperature and the co-crystal former is a solid at room temperature; and wherein
- b) the API and co-crystal former are hydrogen bonded to each other; and
- c) specifically excluding a co-crystal selected from the group consisting of: nabumetone:2,3-naphthalenediol, fluoxetine HCl:benzoic acid, fluoxetine HCl:succinic acid, acetaminophen:piperazine, acetaminophen:theophylline, theophylline:salicylic acid, theophylline:p-hydroxybenzoic acid, theophylline:sorbic acid, theophylline:1-hydroxy-2-naphthoic acid, theophylline:glycolic acid, theophylline:2,5-dihydroxybenzoic acid, theophylline:chloroacetic acid, bis(diphenylhydantoin):9-ethyladenine acetylacetone solvate, bis(diphenylhydantoin):9-ethyladenine 2,4-pentanedione solvate, 5,5-diphenylbarbituric acid:9-ethyladenine, bis(diphenylhydantoin):9-ethyladenine, 4-aminobenzoic acid:4-aminobenzonitrile, sulfadimidine:salicylic acid, 8-hydroxyquinolinium 4-nitrobenzoate:4-nitrobenzoic acid, sulfaproxyline:caffeine, retro-inverso-isopropyl (2R,3S)-4-cyclohexyl-2-hydroxy-3-(N-((2R)-2-morpholinocarbonylmethyl-3-(1-naphthyl)propionyl)-L-histidylamino)butyrate:cinnamic acid monohydrate, benzoic acid:isonicotinamide, 3-(2-N',N'-(dimethylhydrazino)-4-thiazolylmethylthio)-N''-sulfamoylpropionamidine:maleic acid, diglycine hydrochloride (C₂H₅NO₂:C₂H₆NO₂⁺Cl⁻), octadecanoic acid:3-pyridinecarboxamide, cis-N-(3-methyl-1-(2-(1,2,3,4-tetrahydro)naphthyl)-piperidin-4-yl)-N-phenylpropanamide hydrochloride:oxalic acid, trans-N-(3-methyl-1-(2-(1,2,3,4-tetrahydro)naphthyl)-piperidin-4-yl)-N-phenylpropanamide oxalate:oxalic acid dihydrate, bis(1-(3-((4-(2-isopropoxyphenyl)-1-piperazinyl)methyl)benzoyl)piperidine) succinate:succinic acid, bis(p-cyanophenyl)imidazolylmethane:succinic acid, cis-1-((4-(1-imidazolylmethyl)cyclohexyl)methyl)imidazole:succinic acid, (+)-2-(5,6-dimethoxy-1,2,3,4-tetrahydro-1-naphthyl)imidazoline:(+)-dibenzoyl-D-tartaric acid, raclopride:tartaric acid, 2,6-diamino-9-ethylpurine:5,5-diethylbarbituric acid, 5,5-diethylbarbituric acid:bis(2-aminopyridine).

5,5-diethylbarbituric acid:acetamide, 5,5-diethylbarbituric acid:KI₃, 5,5-diethylbarbituric acid:urea,
bis(barbital):hexamethylphosphoramide, 5,5-diethylbarbituric acid:imidazole, barbital:1-
methylimidazole, 5,5-diethylbarbituric acid:N-methyl-2-pyridone, 2,4-diamino-5-(3,4,5-
trimethoxybenzyl)-pyrimidine:5,5-diethylbarbituric acid, bis(barbital):caffeine, bis(barbital):1-
methylimidazole, bis(beta-cyclodextrin):bis(barbital) hydrate, tetrakis(beta-
cyclodextrin):tetrakis(barbital), 9-ethyladenine:5,5-diethylbarbituric acid, barbital:N'-(p-
cyanophenyl)-N-(p-iodophenyl)melamine, barbital:2-amino-4-(m-bromophenylamino)-6-chloro-
1,3,5-triazine, 5,5-diethylbarbituric acid:N,N'-diphenylmelamine, 5,5-diethylbarbituric acid:N,N'-
bis(p-chlorophenyl)melamine, N,N'-bis(p-bromophenyl)melamine:5,5-diethylbarbituric acid, 5,5-
diethylbarbituric acid:N,N'-bis(p-iodophenyl)melamine, 5,5-diethylbarbituric acid:N,N'-bis(p-
tolyl)melamine, 5,5-diethylbarbituric acid:N,N'-bis(m-tolyl)melamine, 5,5-diethylbarbituric
acid:N,N'-bis(m-chlorophenyl)melamine, N,N'-Bis(m-methylphenyl)melamine:barbital, N,N'-
bis(m-chlorophenyl)melamine:barbital tetrahydrofuran solvate, 5,5-diethylbarbituric acid:N,N'-bis(t-
butyl)melamine, 5,5-diethylbarbituric acid:N,N'-di(t-butyl)melamine, 6,6'-diquinolyl ether:5,5-
diethylbarbituric acid, 5-t-butyl-2,4,6-triaminopyrimidine:diethylbarbituric acid, N,N'-bis(4-
carboxymethylphenyl)melamine:barbital ethanol solvate, N,N'-bis(4-t-
butylphenyl)melamine:barbital, tris(5,17-N,N'-bis(4-amino-6-(butylamino)-1,3,5-triazin-2-
yl)diamino-11,23-dinitro-25,26,27,28-tetrapropoxycalix(4)arene):hexakis(diethylbarbituric acid)
toluene solvate, N,N'-bis(m-fluorophenyl)melamine:barbital, N,N'-bis(m-
bromophenyl)melamine:barbital acetone solvate, N,N'-bis(m-iodophenyl)melamine:barbital
acetonitrile solvate, N,N'-bis(m-trifluoromethylphenyl)melamine:barbital acetonitrile solvate,
aminopyrine:barbital, N,N'-bis(4-fluorophenyl)melamine:barbital, N,N'-bis(4-
trifluoromethylphenyl)melamine:barbital, 2,4-diamino-5-(3,4,5-
trimethoxybenzyl)pyrimidine:barbital, hydroxybutyrate:hydroxyvalerate, 2-
aminopyrimidine:succinic acid, 1,3-bis(((6-methylpyrid-2-yl)amino)carbonyl)benzene:glutaric acid,
5-t-butyl-2,4,6-triaminopyrimidine:diethylbarbituric acid, bis(dithiobiuret-S,S')nickel(II):diuracil,
platinum 3,3'-dihydroxymethyl-2,2'-bipyridine dichloride:AgF₃CSO₃, 4,4'-bipyridyl:isophthalic
acid, 4,4'-bipyridyl:1,4-naphthalenedicarboxylic acid, 4,4'-bipyridyl:1,3,5-cyclohexane-tricarboxylic
acid, 4,4'-bipyridyl:tricarballic acid, urotropin:azelaic acid, insulin:C8-HI (octanoyl-N^c-LysB29-

human insulin), isonicotinamide:cinnamic acid, isonicotinamide:3-hydroxybenzoic acid, isonicotinamide:3-N,N-dimethylaminobenzoic acid, isonicotinamide:3,5-bis(trifluoromethyl)-benzoic acid, isonicotinamide:d,l-mandelic acid, isonicotinamide:chloroacetic acid, isonicotinamide:fumaric acid monoethyl ester, isonicotinamide:12-bromododecanoic acid, isonicotinamide:fumaric acid, isonicotinamide:succinic acid, isonicotinamide:4-ketopimelic acid, isonicotinamide:thiodiglycolic acid, 1,3,5-cyclohexane-tricarboxylic acid:hexamethyltetramine, 1,3,5-cyclohexane-tricarboxylic acid:4,7-phenanthroline, 4,7-phenanthroline:oxalic acid, 4,7-phenanthroline:terephthalic acid, 4,7-phenanthroline: 1,3,5-cyclohexane-tricarboxylic acid, 4,7-phenanthroline:1,4-naphthalenedicarboxylic acid, pyrazine:methanoic acid, pyrazine:ethanoic acid, pyrazine:propanoic acid, pyrazine:butanoic acid, pyrazine:pentanoic acid, pyrazine:hexanoic acid, pyrazine:heptanoic acid, pyrazine:octanoic acid, pyrazine:nonanoic acid, pyrazine:decanoic acid, diammine-(deoxy-quanyl-quanyl-N⁷,N⁷)-platinum:tris(glycine) hydrate, 2-aminopyrimidine:p-phenylenediacetic acid, bis(2-aminopyrimidin-1-ium)fumarate:fumaric acid, 2-aminopyrimidine:indole-3-acetic acid, 2-aminopyrimidine:N-methylpyrrole-2-carboxylic acid, 2-aminopyrimidine:thiophen-2-carboxylic acid, 2-aminopyrimidine:(+)-camphoric acid, 2,4,6-Trinitrobenzoic acid: 2-aminopyrimidine, 2-aminopyrimidine:4-aminobenzoic acid, 2-aminopyrimidine:bis(phenoxyacetic acid), 2-aminopyrimidine:(2,4-dichlorophenoxy)acetic acid, 2-aminopyrimidine:(3,4-dichlorophenoxy)acetic acid, 2-aminopyrimidine:indole-2-carboxylic acid, 2-aminopyrimidine:terephthalic acid, 2-aminopyrimidine:bis(2-nitrobenzoic acid), 2-aminopyrimidine:bis(2-aminobenzoic acid), 2-aminopyrimidine:3-aminobenzoic acid, 2-hexeneoic acid:isonicotinamide, 4-nitrobenzoic acid:isonicotinamide, 3,5-dinitrobenzoic acid:isonicotinamide:4-methylbenzoic acid, 2-amino-5-nitropyrimidine:2-amino-3-nitropyridine, 3,5-dinitrobenzoic acid:4-chlorobenzamide, 3-dimethylaminobenzoic acid:4-chlorobenzamide, fumaric acid:4-chlorobenzamide, oxine:4-nitrobenzoic acid, oxine:3,5-dinitrobenzoic acid, oxine:3,5-dinitrosalicylic acid, 3-[2-(N',N'-dimethylhydrazino)-4-thiazolylmethylthio]-N²-sulfamoylpropionamide:maleic acid, 5-fluorouracil:9-ethylhypoxanthine, 5-fluorouracil:cytosine dihydrate, 5-fluorouracil:theophylline monohydrate, stearic acid:nicotinamide, cis-1-{[4-(1-imidazolylmethyl)cyclohexyl]methyl}imidazole:succinic acid, CGS18320B:succinic acid, sulfaproxyline:caffeine, 4-aminobenzoic acid:4-aminobenzonitrile, 3,5-dinitrobenzoic

acid:isonicotinamide:3-methylbenzoic acid, 3,5-dinitrobenzoic acid:isonicotinamide:4-(dimethylamino)benzoic acid, 3,5-dinitrobenzoic acid:isonicotinamide:4-hydroxy-3-methoxycinnamic acid, isonicotinamide:oxalic acid, isonicotinamide:malonic acid, isonicotinamide:succinic acid, isonicotinamide:glutaric acid, isonicotinamide:adipic acid, benzoic acid:isonicotinamide, mazapertine:succinate, betaine:dichloronitrophenol, betainepyridine:dichloronitrophenol, betainepyridine:pentachlorophenol, 4-{2-[1-(2-hydroxyethyl)-4-pyridylidene]-ethylidene}-cyclo-hexa-2,5-dien-1-one:methyl 2,4-dihydroxybenzoate, 4-{2-[1-(2-hydroxyethyl)-4-pyridylidene]-ethylidene}-cyclo-hexa-2,5-dien-1-one:2,4-dihydroxypropiophenone, 4-{2-[1-(2-hydroxyethyl)-4-pyridylidene]-ethylidene}-cyclo-hexa-2,5-dien-1-one:2,4-dihydroxyacetophenone, squaric acid:4,4'-dipyridylacetylene, squaric acid:1,2-bis(4-pyridyl)ethylene, chloranilic acid:1,4-bis[(4-pyridyl)ethynyl]benzene, 4,4'-bipyridine:phthalic acid, 4,4'-dipyridylacetylene:phthalic acid, bis(pentamethylcyclopentadienyl)iron:bromanilic acid, bis(pentamethylcyclopentadienyl)iron:chloranilic acid, bis(pentamethylcyclopentadienyl)iron:cyananilic acid, pyrazinotetrathiafulvalene:chloranilic acid, phenol:pentafluorophenol, co-crystals of itraconazole, and co-crystals of topiramate or hydrochlorothiazide.

2 (original). The pharmaceutical co-crystal composition according to claim 1, wherein:

- (a) the co-crystal former is selected from a co-crystal former of Table I or Table II;
- (b) the API is selected from an API of Table IV;
- (c) the API is selected from an API of Table IV and the co-crystal former is selected from a co-crystal former of Table I or Table II;
- (d) the API is a liquid at room temperature;
- (e) the API is a solid at room temperature;
- (f) the API has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp² amine, thiocyanate, cyanamide, oxime,

nitrile, diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine;

- (g) the co-crystal former has at least one functional group selected from the group consisting of ether, thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, sp² amine, thiocyanate, cyanamide, oxime, nitrile diazo, organohalide, nitro, s-heterocyclic ring, thiophene, n-heterocyclic ring, pyrrole, o-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine;
- (h) the difference in pK_a between the API and the co-crystal former does not exceed 2;
- (i) the solubility of the co-crystal is increased as compared to the API;
- (j) the dose response of the co-crystal is increased as compared to the API;
- (k) the dissolution of the co-crystal is increased as compared to the API;
- (l) the bioavailability of the co-crystal is increased as compared to the API;
- (m) the stability of the co-crystal is increased as compared to the API;
- (n) a difficult to salt or unsaltable API is incorporated into the co-crystal;
- (o) the hygroscopicity of the co-crystal is decreased as compared to the API;
- (p) an amorphous API is crystallized as a component of the co-crystal;
- (q) the form diversity of the co-crystal is decreased as compared to the API; or
- (r) the morphology of the co-crystal is modulated as compared to the API.

3-8 (canceled).

9 (currently amended). The pharmaceutical co-crystal composition according to claim 1, wherein the API is selected from celecoxib, carbamazepine, ~~itraconazole~~, olanzapine, topiramate,

modafinil, 5-fluorouracil, ~~hydrochlorothiazide~~, acetaminophen, aspirin, flurbiprofen, phenytoin, or ibuprofen.

10 (original). The pharmaceutical co-crystal composition according to claim 1, further comprising a pharmaceutically acceptable diluent, excipient, or carrier.

11 (currently amended). A co-crystal comprising an API and a co-crystal former selected from:

- (a) carbamazepine and saccharin;
- (b) carbamazepine and nicotinamide;
- (c) carbamazepine and trimesic acid;
- (d) celecoxib and nicotinamide;
- (e) olanzapine and nicotinamide;
- (f) celecoxib and 18-crown-6;
- ~~(g) itraconazole and succinic acid;~~
- ~~(h) itraconazole and fumaric acid;~~
- ~~(i) itraconazole and tartaric acid;~~
- ~~(j) itraconazole and malic acid;~~
- ~~(k)(g)~~ _____ itraconazoleHCl and tartaric acid;
- ~~(l)(h)~~ _____ modafinil and malonic acid;
- ~~(m)(i)~~ _____ modafinil and benzamide;
- ~~(n)(j)~~ _____ modafinil and mandelic acid;
- ~~(o)(k)~~ _____ modafinil and glycolic acid;
- ~~(p)(l)~~ _____ modafinil and fumaric acid;
- ~~(q)(m)~~ _____ modafinil and maleic acid;
- ~~(r) topiramate and 18-crown-6;~~
- ~~(s)(n)~~ _____ 5-fluorouracil and urea;
- ~~(t) hydrochlorothiazide and nicotinic acid;~~
- ~~(u) hydrochlorothiazide and 18-crown-6;~~

~~(v)~~hydrochlorothiazide and piperazine;
~~(w)~~(o) _____ acetaminophen and 4,4'-bipyridine;
~~(x)~~(p) _____ phenytoin and pyridone;
~~(y)~~(q) _____ aspirin and 4,4'-bipyridine;
~~(z)~~(r) _____ ibuprofen and 4,4'-bipyridine;
~~(aa)~~(s) _____ flurbiprofen and 4,4'-bipyridine;
~~(bb)~~(t) _____ flurbiprofen and trans-1,2-bis(4-pyridyl) ethylene;
~~(cc)~~(u) _____ carbamazepine and p-phthalaldehyde;
~~(dd)~~(v) _____ carbamazepine and 2,6-pyridinecarboxylic acid;
~~(ee)~~(w) _____ carbamazepine and 5-nitroisophthalic acid;
~~(ff)~~(x) _____ carbamazepine and 1,3,5,7-adamantane tetracarboxylic acid; or
~~(gg)~~(y) _____ carbamazepine and benzoquinone.

12-37 (canceled).

38 (new). The pharmaceutical co-crystal composition according to claim 1, wherein:

(a) the API comprises an amide, an amine or a carboxylic acid group as hydrogen bonded moiety and the co-crystal former comprises aldehyde, amide, carboxylic acid, ketone or pyridine group as hydrogen bonded moiety, or

(b) the API comprises an aldehyde, aromatic nitrogen, ether or sulfonyl group as hydrogen bonded moiety and the co-crystal former comprises amide, carboxylic acid or pyridine as hydrogen bonded moiety, or

(c) the API comprises an alcohol, organochloride group as hydrogen bonded moiety and the co-crystal former comprises amide, carboxylic acid or pyridine as hydrogen bonded moiety, or

(d) one of said API and said co-crystal former comprises an alcohol, aldehyde, amide, secondary amine, carboxylic acid, ether, ester, ketone, nitrile, organochloride pyridine, sulfonyl or sulfonamide group as hydrogen bonded moiety and the other of said API and co-crystal former comprises aldehyde, amide, carboxylic acid, ketone or pyridine as hydrogen-bonded moiety.

39 (new). The pharmaceutical co-crystal composition according to claim 38, wherein the API comprises an amide, an amine or a carboxylic acid group as hydrogen bonded moiety and the co-crystal former comprises aldehyde, amide, carboxylic acid, ketone or pyridine group as hydrogen bonded moiety.

40 (new). The pharmaceutical co-crystal composition according to claim 38, wherein the API comprises an aldehyde, aromatic nitrogen, ether or sulfonyl group as hydrogen bonded moiety and the co-crystal former comprises amide, carboxylic acid or pyridine as hydrogen bonded moiety.

41 (new). The pharmaceutical co-crystal composition according to claim 38, wherein the API comprises an alcohol, organochloride group as hydrogen bonded moiety and the co-crystal former comprises amide, carboxylic acid or pyridine as hydrogen bonded moiety.

42 (new). The pharmaceutical co-crystal composition according to claim 38, wherein one of said API and said co-crystal former comprises an alcohol, aldehyde, amide, secondary amine, carboxylic acid, ether, ester, ketone, nitrile, organochloride pyridine, sulfonyl or sulfonamide group as hydrogen bonded moiety and the other of said API and co-crystal former comprises aldehyde, amide, carboxylic acid, ketone or pyridine as hydrogen-bonded moiety.